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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/308,027	08/16/1999	TOSHIO SONE	06501/031001	5615

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EXAMINER
HUYNH, PHUONG N

ART UNIT	PAPER NUMBER
1644	16

DATE MAILED: 03/12/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/308,027	SONE ET AL.	
	Examiner	Art Unit	
	" Neon" Phuong Huynh	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *Three* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12/11/000; 1/10/02* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *16 and 17* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *16-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *5, 6 & 7* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Claims 16-17 are pending.

2. Claims 16-17 are being acted upon in this Office Action.

3. Applicant should amend the first line of the specification to reflect the relationship between the instant application and PCT/JP97/04129 filed 11/12/1997 stated on the oath.

4. The drawings, filed 8/16/99, are not approved. Please see enclosed PTO 948, Notice of Draftsperson's Patent Drawing Review. Appropriate action is required.

5. Claims 16-17 are objected to because of typographical error "DQB1*0501"; the specification discloses on page 13, item 5 that it is "DPB1*0501". Appropriate action is required.

6. The disclosure is objected to because of the following informality: "IF-Nγ" on page 27, line 8 should have been "IFN-γ". Appropriate action is required.

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 16-17 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling only for (1) A method for **treating** allergy in a patient suffering from a cedar pollen allergy wherein the method comprising (a) identifying an HLA class II molecule expressed by the patient; (b) selecting an antigenic peptide derived from Japanese cedar pollen allergen Cry J j 1 or Japanese cedar pollen allergen Cry j2 wherein the antigenic peptide binds to the HLA class II molecule and wherein: (1) when the HLA class II molecule identified in step (a) is DQA1*0102-DQB1*0601, the antigenic peptide is selected from the group consisting of SEQ ID NO: 1, 5, 7, 9, 10, 21 and 23; (2) when the HLA class II molecule identified in step (a) is DPA1*0101-DPB1*0501, the antigenic peptide is selected from the group consisting of SEQ ID NO: 2, 8 and 15; (3) when the HLA class II molecule identified in step (a) is DPA1*0101-

DPB1*0201, the antigenic peptide is selected from the group consisting of SEQ ID NO: 17; (4) when the HLA class II molecule identified in step (a) is DPA1*0202-DPB1*0501, the antigenic peptide is SEQ ID NO: 22; (5) when the HLA class II molecule identified in step (a) is DRB5*0101, the antigenic peptide is SEQ ID NO: 3, 4, 14 and 19; (6) when the HLA class II molecule identified in step (a) is DRB1*0901, the antigenic peptide is SEQ ID NO: 6, 7, 12, 16 and 20 and (7) when the HLA class II molecule identified in step (a) is DRB4*0101, the antigenic peptide is SEQ ID NO: 7 and 18; and (8) when the HLA class II molecule identified in step (a) is DRB1-1501, the antigenic peptide is SEQ ID NO: 13 and 19; (c) administering the selected antigenic peptide to the patient, does not reasonably provide enablement for (1) *any* methods mentioned above for "**preventing**" allergy in a patient suffering from a cedar pollen allergy; (2) *any* methods mentioned above for "**preventing**" allergy in a patient suffering from a cedar pollen allergy wherein the method comprising (a) identifying an HLA class II molecule expressed by the patient; (b) selecting an antigenic peptide derived from Japanese cedar pollen allergen Cry J j 1 or Japanese cedar pollen allergen Cry j2 wherein the antigenic peptide binds to the HLA class II molecule and wherein: (i) if the HLA class II molecule identified in step (a) is DQA1*0102-DQB1*0601, the antigenic peptide is selected from the group consisting of SEQ ID NO: **25**; (ii) if the HLA class II molecule identified in step (a) is DPA1*0202-**DQB1***0501, the antigenic peptide is SEQ ID NO: 22 and (iii) if the HLA class II molecule identified in step (a) is DRB4*0101, the antigenic peptide is **SEQ ID NO: 12**; (c) administering the selected antigenic peptide to the patient using (3) said customized pharmaceutical composition. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in **scope** with these claims.

Factors to be considered in determining whether undue experimentation is required to practice the claimed invention are summarized *In re Wands* (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). The factors most relevant to this rejection are the scope of the claim, the amount of direction or guidance provided, the lack of sufficient working examples, the unpredictability in the art and the amount of experimentation required to enable one of skill in the art to practice the claimed invention. The specification disclosure is insufficient to enable one skilled in the art to practice the invention as broadly claimed without an undue amount of experimentation.

The specification discloses only a method for "**treating**" allergy in a patient suffering from a cedar pollen allergy mentioned above wherein the method comprising (a) identifying an

HLA class II molecule expressed by the patient; (b) selecting an antigenic peptide derived from Japanese cedar pollen allergen Cry j 1 or Japanese cedar pollen allergen Cry j2 using T-cell cell lines recognizes Cry j 1 or Cry j 2 and (c) administering said pharmaceutical composition to a patient.

Other than the specific peptides correlated with the specific HLA molecule mentioned above for a method for **treating** cedar pollen allergy using said peptide as a pharmaceutical composition, there is insufficient guidance and working examples of using a customized pharmaceutical composition comprising an antigenic peptide of **SEQ ID NO: 25** if the patient expresses HLA class II molecule DQA1*0102-DQB1*0501 or an antigenic peptide of SEQ ID NO: 22 if the HLA class II molecule identified is **DQB1***0501, or an antigenic peptide of **SEQ ID NO: 12** if the HLA class II molecule identified is DRB4*0101 since the specification as filed fails to teach the specific amino acid residues of the antigenic peptide of SEQ ID NO: 25 or 12 derived from Japanese Cedar pollen allergen. Given the indefinite number of undisclosed peptide and the heterogeneous MHC class II molecule in a given population, it is unpredictable which peptide would be useful for a customized pharmaceutical composition, in turn, for a method of treating a patient suffering from a cryptomeria pollen allergy.

Further, the specification does not teach a method for "**preventing**" allergy in a patient suffering from a cedar pollen allergy using any mentioned above. The term "preventing" means to averting or to keep from happening as defines by Webster's II New Riverside University Dictionary on page 933. There is insufficient guidance and working examples using any peptide mentioned above for "preventing" cedar pollen allergy from *any* individual. Furthermore, the is no support of using the peptide of SEQ ID NO: 25 in the specification or the claims as originally filed for a method of treating or preventing allergy in a patient suffering from a cedar pollen allergy wherein the patient's HLA class II molecule is DQA1*102-DQB1*0602. Likewise, the specification or the claim as originally filed does not have support for using peptide of **SEQ ID NO: 22** for a method of treating or preventing allergy in a patient suffering from a cedar pollen allergy wherein the patient's HLA class II molecule is **DQB1***0501. Finally, the specification or the claims as originally filed does not have support for using peptide of **SEQ ID NO: 12** for a method of treating or preventing allergy in a patient suffering from a cedar pollen allergy wherein the patient's HLA class II molecule is DRB1*1501. Given the lack of guidance with respect to the specific peptides mentioned above for a method of treating or preventing a patient suffering from a cedar pollen allergy, it is unpredictable whether said peptides would be useful and

effective as a customized peptide-based immunotherapeutic composition for treating or preventing allergy associated with cedar pollen in any individual given that HLA class II molecules in human are very diverse and polymorphic.

Hoyne *et al* teach the success of peptide based hyposensitization therapy depends on the decrease of T cell response such as a decrease in Th2 type cytokine production by allergen specific Th cells or allergen derived peptide that are recognized by specific CD4+ T cells. There are a number of problems that need to be addressed before peptides can make the transition from experimental systems to clinical application such as peptides containing immunodominant epitopes are more potent tolergens than those containing minor epitopes. In order to obtain information on the distribution of immunodominant T cell epitopes for a particular allergen, it will be necessary to perform detailed epitope analysis on the peripheral repertoire of a large panel of allergic patients of known HLA haplotypes (See page 184, second paragraph, in particular). Since recognition of peptide epitopes by T cells is dependent on the presentation of peptide by appropriate MHC molecule and for maximum efficacy, the peptide should be short and selected on the basis of their ability to bind to MHC molecules. Given that the binding specificity of the claimed peptide to MHC molecule is unknown and because the claimed composition does not match the MHC class II molecule and vice versa as taught in the specification, further experimentation is required to practice the claimed invention.

In re wands, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988), the decision of the court indicates that the more unpredictable the area is, the more specific enablement is necessary. In view of the quantity of experimentation necessary, the limited working examples, the unpredictability of the art, the lack of sufficient guidance in the specification and the breadth of the claims, it would take an undue amount of experimentation for one skilled in the art to practice the claimed invention.

9. Claims 16-17 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

The specification does not reasonably provide a **written description** for *any* methods mentioned above for "**preventing**" allergy in a patient suffering from a cedar pollen allergy; (2) *any* methods mentioned above for treating or "**preventing**" allergy in a patient suffering from a

cedar pollen allergy wherein the method comprising (a) identifying an HLA class II molecule expressed by the patient; (b) selecting an antigenic peptide derived from Japanese cedar pollen allergen Cry j 1 or Japanese cedar pollen allergen Cry j2 wherein the antigenic peptide binds to the HLA class II molecule and wherein: (i) if the HLA class II molecule identified in step (a) is DQA1*0102-DQB1*0601, the antigenic peptide is selected from the group consisting of SEQ ID NO: **25**; (ii) if the HLA class II molecule identified in step (a) is DPA1*0202-**DQB1***0501, the antigenic peptide is SEQ ID NO: 22 and (iii) if the HLA class II molecule identified in step (a) is DRB4*0101, the antigenic peptide is **SEQ ID NO: 12**; (c) administering the selected antigenic peptide to the patient using said customized pharmaceutical composition.

The specification discloses only (1) A method for **treating** allergy in a patient suffering from a cedar pollen allergy wherein the method comprising (a) identifying an HLA class II molecule expressed by the patient; (b) selecting an antigenic peptide derived from Japanese cedar pollen allergen Cry j1 or Japanese cedar pollen allergen Cry j2 wherein the antigenic peptide binds to the HLA class II molecule and wherein: (1) when the HLA class II molecule identified in step (a) is DQA1*0102-DQB1*0601, the antigenic peptide is selected from the group consisting of SEQ ID NO: 1, 5, 7, 9, 10, 21 and 23; (2) when the HLA class II molecule identified in step (a) is DPA1*0101-DPB1*0501, the antigenic peptide is selected from the group consisting of SEQ ID NO: 2, 8 and 15; (3) when the HLA class II molecule identified in step (a) is DPA1*0101-DPB1*0201, the antigenic peptide is selected from the group consisting of SEQ ID NO: 17; (4) when the HLA class II molecule identified in step (a) is DPA1*0202-DPB1*0501, the antigenic peptide is SEQ ID NO: 22; (5) when the HLA class II molecule identified in step (a) is DRB5*0101, the antigenic peptide is SEQ ID NO: 3, 4, 14 and 19; (6) when the HLA class II molecule identified in step (a) is DRB1*0901, the antigenic peptide is SEQ ID NO: 6, 7, 12, 16 and 20 and (7) when the HLA class II molecule identified in step (a) is DRB4*0101, the antigenic peptide is SEQ ID NO: 7 and 18; and (8) when the HLA class II molecule identified in step (a) is DRB1-1501, the antigenic peptide is SEQ ID NO: 13 and 19; (c) administering the selected antigenic peptide to the patient. There is insufficient written description about the structure and function of peptide of SEQ ID NO: 25 and 12. There is also insufficient written description about whether MHC class II molecule **DQB1*0501** is appropriated for peptide SEQ ID NO: 22 for a customized pharmaceutical composition for a method of treating or preventing allergy in a patient suffering from a cedar pollen allergy.

Applicant is directed to the Revised Interim Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

10. Claims 16 and 17 are rejected under 35 U.S.C. 112, first paragraph, containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **This is a new matter rejection.**

The "SEQ ID NO: 25" in claim 16(1) and claim 17(1) represents a departure from the specification and the claims as originally filed. The specification discloses on page 13 that if the HLA class II molecule identified in step (a) is DQA1*0102-DQB1*0601, the antigenic peptide is selected from the group consisting of SEQ ID NO: 1, 5, 7, 9, 10, 21 and 23.

The "SEQ ID NO: 12" in claim 16(7) and claim 17(7) represents a departure from the specification and the claims as originally filed. The specification discloses on page 13 that if HLA class II molecule identified in step (a) is DRB4*0101, the antigenic peptide is SEQ ID NO: 7 and 18.

The "DQB1*0501" in claim 16(4) and claim 17 (4) represents a departure from the specification and the claims as originally filed. The specification discloses on page 14, line 5 from the bottom of the page that if the HLA class II molecule identified in step (a) is DPA1*0202-DPB1*0501, the antigenic peptide is SEQ ID NO: 22.). Applicant has not pointed out where the supports come from.

11. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

12. Claims 16-17 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The recitation of "if" in Claims 16-17 is indefinite and ambiguous. One of ordinary skill in the art cannot appraise the metes and bounds of the claimed invention. Appropriate action is required. Appropriate correction is required.

INFORMATION ON HOW TO EFFECT DRAWING CHANGES

1. Correction of Informalities -- 37 CFR 1.85

New corrected drawings must be filed with the changes incorporated therein. Identifying indicia, if provided, should include the title of the invention, inventor's name, and application number, or docket number (if any) if an application number has not been assigned to the application. If this information is provided, it must be placed on the front of each sheet and centered within the top margin. If corrected drawings are required in a Notice of Allowability (PTOL-37), the new drawings **MUST** be filed within the **THREE MONTH** shortened statutory period set for reply in the "Notice of Allowability." Extensions of time may NOT be obtained under the provisions of 37 CFR 1.136 for filing the corrected drawings after the mailing of a Notice of Allowability. The drawings should be filed as a separate paper with a transmittal letter addressed to the Official Draftsperson.

2. Corrections other than Informalities Noted by Draftsperson on form PTO-948.

All changes to the drawings, other than informalities noted by the Draftsperson, **MUST** be made in the same manner as above except that, normally, a highlighted (preferably red ink) sketch of the changes to be incorporated into the new drawings **MUST** be approved by the examiner before the application will be allowed. No changes will be permitted to be made, other than correction of informalities, unless the examiner has approved the proposed changes.

3. Timing of Corrections

Applicant is required to submit acceptable corrected drawings within the time period set in the Office action. See 37 CFR 1.85(a). Failure to take corrective action within the set period will result in **ABANDONMENT** of the application.

13. No claim is allowed.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to "Neon" Phuong Huynh whose telephone number is (703) 308-4844. The examiner can normally be reached Monday through Friday from 9:00 am to 6:00 p.m. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

15. Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform to the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-7401.

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Patent Examiner
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March 11, 2002

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